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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,464	12/20/2001	Sheila J. Kelly	1416.07US01	1559

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EXAMINER	
FORD, ALLISON M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 08/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/027,464	KELLY ET AL.	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8-11 and 16-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8-11 and 16-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response of 11 July 2006 has been received and entered into the case. Claims 1 and 8 have been amended. Claims 6, 7, 12-15 and 28-40 have been cancelled. Claims 1-5, 8-11 and 16-27 remain pending in the current application, all of which have been examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 9-11 and 16-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It has been held that "an applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention... one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process." MPEP § 2163

In the instant application the claims are directed a composite matrix comprising a first layer and a second layer, each layer having a flexibility modifying agent in specified quantities, and wherein the flexibility modifying agent comprises an elastic protein. With regards to the 'flexibility modifying agent' the specification teaches that the flexibility modifying agent can be bio-macromolecules, such as elastin

and proteoglycans, or synthetic polymers (See spec, page 19), no further species or examples of proteoglycans or synthetic polymers are provided (it is noted that on page 15 applicants disclose numerous synthetic polymers; however, these are only taught as examples of polymeric materials used in composite structures, they are not disclosed as specific species of 'flexibility modifying agents').

However, applicants have now limited the 'flexibility modifying agent' to agents which comprise *an elastic protein*; yet, the instant disclosure still fails to provide sufficient written description of a representative number of species of elastic proteins which is required to claim the genus of 'elastic proteins'. The only discussion of elastic proteins is found on page 22 of the specification, wherein applicants teach "additional components can be added to the composite to alter the mechanical properties of a layer. For example, a layer can include elastin and similar proteins to impart elasticity to the layer. Suitable proteins can be called elastic proteins." Applicants continue to describe the structure of elastin, but are silent with regards to the 'other suitable proteins' which fall into the genus of 'elastic proteins'. Therefore, absent any discussion or disclosure of the 'other suitable proteins' which are considered to be 'elastic proteins', there is not considered to be sufficient evidence the applicants were in possession of the claimed genus of 'elastic proteins', but rather it appears applicants were limited to the single species of elastin, as the only flexibility modifying agent. *See Eli Lilly,* 119F. 3d. at 1568, 43 USPQ2d at 1406. See MPEP § 2163.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 8-11 and 16-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's claims are directed to a composite matrix comprising a first layer and a second layer, each layer having a flexibility modifying agent, the first layer having at least about 5 dry weight percent flexibility modifying agent and the second layer having at least about 5 dry weight percent less flexibility modifying agent than the first layer, wherein at least one layer comprises a reconstituted composition, and wherein the flexibility modifying agent comprises an elastic protein.

In claim 1, it is unclear if the flexibility modifying agent, which is to comprise an elastic protein, must be the same agent in each of the first and second layers. If the flexibility modifying agent is to be the same in the first and second layers, it would be remedial to adopt the language "wherein said first/second layer comprises at least X amount of *said* flexibility modifying agent."

Furthermore, in claim 1, it is not clear what is meant by a 'reconstituted composition', and it is not clear if the reconstituted composition is to be in addition to the flexibility modifying agent, or if the flexibility modifying agent is to be the reconstituted composition. If the 'reconstituted composition' is to be in addition to the flexibility modifying agent, it would be remedial to change the language to, "...wherein at least one of said layers *further* comprises a reconstituted composition..."

Claims 2-5 requires the second layer to comprise collagen in different forms and/or amounts. Because collagen is not considered a flexibility modifying agent, it appears the collagen is to be an additional component; therefore it would be clearer to modify the language of each of the claims to read, "wherein the second layer *further* comprises [collagen]." Claims 10, 23, 25 and 27 also teach additional components and thus for clarity should read, "wherein the first layer *further* comprises...."

Claim 16 is considered unclear, because claim 1, as amended, now requires the flexibility modifying agent to comprise an elastic protein, and claim 16 still requires the addition of elastic proteins. This appears to be repetitive and unnecessary. It appears claim 16 should be amended to read, "The composite material of claim 1 wherein the flexibility modifying agent further comprises friction reducing

macromolecules." However, please note, this change would make claim 16 a substantial duplicate of claim 11, which would be inappropriate.

Claim 26 is considered indefinite because it is not clear what is included as an attachment compound for fibroblasts precursor cells or for vascular endothelial precursor cells.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 8-11, 16, 20-22 and 23-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Ryan (WO 00/35372).

Applicant's claims are directed to a composite matrix comprising a first layer and a second layer, each layer having a flexibility modifying agent, the first layer having at least about 5 dry weight percent flexibility modifying agent and the second layer having at least about 5 dry weight percent less flexibility modifying agent than the first layer, wherein at least one layer comprises a reconstituted composition, and wherein the flexibility modifying agent comprises an elastic protein. Some dependent claims further require the first or second layer to further comprise collagen in different concentrations. Some dependent claims further require the flexibility modifying agent to comprise friction reducing macromolecules (examples of such in the specification include hyaluronic acid and chondroitin sulfate, Pg. 23). Some dependent claims limit the thickness of each layer. Some dependent claims require the first or second layers to further comprise cells, growth factors or cell attachment compounds.

Ryan teaches a method of producing a multilayered blood vessel prosthesis by creating and assembling multiple matrices; Ryan further teaches the multilayered blood vessel prostheses thereby

produced. In a preferred embodiment, Ryan teaches a multilayered blood vessel prosthesis that includes (i) an inner layer comprising type I collagen, type IV collagen, GAG, elastin, and laminin; and (ii) an outer layer comprising type I collagen, GAG, elastin, and fibronectin (See Ryan Pg. 3, ln 11-14). Examples of suitable GAGs include chondroitin-6-sulfate, chondroitin-4-sulfate, heparin sulfate, dermatan sulfate, keratin sulfate, chitosan, hyaluronic acid, heparin and combinations thereof (See Ryan, PG. 5, ln 12-16); thus the GAGs included in each layer are considered 'friction reducing macromolecules' in accordance with the definition provided in the specification (pg. 23) (Claims 11 & 16). A third layer can optionally be included between the first and second layers (See Ryan, pg. 3, ln 16-20) (Claim 22). Endothelial cells, smooth muscle cells, and/or fibroblasts can be seeded on one or all of the layers (See Ryan, Pg. 7, ln 9-18) and cultured, after culturing the layers are assembled concentrically to form the final multilayered blood vessel prosthesis, wherein the inner layer forms the inner tube, and the outer layer forms the outer tube. Thus the first and second layers are adjacent, the layers each contain viable cells, and viable cells inherently secrete growth factors (Claims 11, 16, 21, 23-27).

Ryan teaches each of the matrix layers includes between 50 and 99% collagen; the collagen may be crosslinked to varying degrees depending on the desired mechanical and bioresorptive properties (See Ryan Pg. 8, ln 18-27) (See Ryan, Pg. 8, ln 15-17) (Claims 2-4, 10, 20).

With regards to the elastin content, Ryan teaches each matrix can include up to 30% by weight elastin, preferably between 5 and 20% (See Ryan, Pg. 9, ln 14-16). However, Ryan further teaches that each of the layers/tubes can be manufactured such that the chemical and/or physical compositions are different in each of the tubes, specifically Ryan teaches the inner layer/tube can have a higher concentration of elastin compared to the outer layer/tube (See Ryan Pg. 7, ln 5-9). The instant claims require the second layer to have 'at least about 5 dry weight percent less flexibility modifying agent (elastin) than the first layer', however, because the phrase 'at least about 5 dry weight percent' is not definite, any difference in elastin concentration between the first and second layers is considered to read

on the instant claims. Thus, because Ryan teaches an elastin concentration ranging from 5 to 20% in each matrix layer, wherein the inner layer (first layer) has a higher concentration of elastin than the outer layer (second layer), the difference between the elastin concentrations is considered to be 'at least about 5%', and thus the claims are anticipated (Claims 1 and 9).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 8-11, and 16-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ryan (WO 00/35372).

Applicant's claims are directed to a composite matrix comprising a first layer and a second layer, each layer having a flexibility modifying agent, the first layer having at least about 5 dry weight percent flexibility modifying agent and the second layer having at least about 5 dry weight percent less flexibility modifying agent than the first layer, wherein at least one layer comprises a reconstituted composition, and wherein the flexibility modifying agent comprises an elastic protein. Some dependent claims further require the first or second layer to further comprise collagen in different concentrations. Some dependent claims further require the flexibility modifying agent to comprise friction reducing macromolecules (examples of such in the specification include hyaluronic acid and chondroitin sulfate, Pg. 23). Some dependent claims limit the thickness of each layer. Some dependent claims require the first or second layers to further comprise cells, growth factors or cell attachment compounds.

Ryan teaches a method of producing a multilayered blood vessel prosthesis by creating and assembling multiple matrices; Ryan further teaches the multilayered blood vessel prostheses thereby

produced. In a preferred embodiment, Ryan teaches a multilayered blood vessel prosthesis that includes (i) an inner layer comprising type I collagen, type IV collagen, GAG, elastin, and laminin; and (ii) an outer layer comprising type I collagen, GAG, elastin, and fibronectin (See Ryan Pg. 3, ln 11-14). Examples of suitable GAGs include chondroitin-6-sulfate, chondroitin-4-sulfate, heparin sulfate, dermatan sulfate, keratin sulfate, chitosan, hyaluronic acid, heparin and combinations thereof (See Ryan, PG. 5, ln 12-16); thus the GAGs included in each layer are considered 'friction reducing macromolecules' in accordance with the definition provided in the specification (pg. 23) (Claims 11 & 16). A third layer can optionally be included between the inner (first) and outer (second) layers (See Ryan, pg. 3, ln 16-20) (Claim 22). Endothelial cells, smooth muscle cells, and/or fibroblasts can be seeded on one or all of the layers (See Ryan, Pg. 7, ln 9-18) and cultured, after culturing the layers are assembled concentrically to form the final multilayered blood vessel prosthesis, wherein the inner layer forms the inner tube, and the outer layer forms the outer tube. Thus the first and second layers are adjacent, the layers each contain viable cells, and viable cells inherently secrete growth factors (Claims 11, 16, 21, 23-27).

Ryan teaches each of the matrix layers includes between 50 and 99% collagen; the collagen may be crosslinked to varying degrees depending on the desired mechanical and bioresorptive properties (See Ryan Pg. 8, ln 18-27) (See Ryan, Pg. 8, ln 15-17) (Claims 2-4, 10, 20). Though Ryan is silent with regards to the source of the collagen, intestinal collagen would have been an obvious design choice, especially in the absence of evidence showing that the source of the collagen affects the patentability of the final composition (Claim 5).

With regards to the elastin content, Ryan teaches each matrix can include up to 30% by weight elastin, preferably between 5 and 20% (See Ryan, Pg. 9, ln 14-16). However, Ryan further teaches that each of the layers/tubes can be manufactured such that the chemical and/or physical compositions are different in each of the tubes, specifically Ryan teaches the inner layer/tube can have a higher concentration of elastin compared to the outer layer/tube (See Ryan Pg. 7, ln 5-9). Ryan is silent as to the

exact difference between the elastin concentrations in each layer; however, he does provide the general teaching that there is to be a difference between the two layers. Therefore, it would have been well within the purview of one of ordinary skill in the art to optimize the concentration of elastin in each matrix layer, and the corresponding difference between the concentrations, as a matter of routine experimentation. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical or produces unexpected results. Where the general conditions of a claim are disclosed by the prior art it is not inventive to discover the optimum or workable ranges by routine experimentation, See *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Also note that where the claimed ranges overlap or lie inside ranges disclosed by the prior art a prima facie case of obviousness exists. See *In re Wertheim,* 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff,* 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990) (Claims 1 and 9).

With regards to the thickness of each of the layers, it is noted that in Example 2, Ryan teach creating individual matrices, which are later used to form the layers, with a thickness of 0.005 inches (127 microns) (See Ryan, Pg. 14, ln 17-18). Therefore, it would have been obvious to one of ordinary skill in the art, in making the product of Ryan, to produce individual layers each with a thickness of approximately 127 microns (Claims 17-19). Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

In the response of 11 July 2006 applicants incorporated the limitations of claim 7 into independent claim 1 in order to over come the rejection of record, as Spiro et al (US Pat, 6,773,723) does not teach or suggest a composite matrix comprising an elastic protein. The amendment to claim 1 obviates the rejections of record; however, new grounds of rejection are presented above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Allison M Ford
Examiner
Art Unit 1651

LEON B. LANKFORD, JR.
PRIMARY EXAMINER